Physical Principles of MR Angiography

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The most widely used MR angiographic imaging techniques can be categorized as *phase contrast*, *time-of-flight*, or *contrast-enhanced* methods. The basic physical principles of each of these techniques are described briefly below.

Phase contrast techniques derive contrast between flowing blood and stationary tissues by manipulating the phase of the magnetization, such that the phase of the magnetization from the stationary spins is zero and that from the moving spins is non-zero. The phase is a measure of how far the magnetization precesses, or rotates, from the time it is tipped into the transverse plane until the time it is detected. The data acquired with phase contrast techniques can be processed to produce phase difference, complex difference, and magnitude images.

In *phase difference* images, the signal is linearly proportional to the velocity of the spins - faster moving spins give rise to a larger signal, and spins moving in one direction are assigned a bright (white) signal, whereas spins moving in the opposite direction are assigned a dark (black) signal. This characteristic of phase difference images permits arteries to be effectively differentiated from veins when they are aligned anti-parallel to each other, as is the case with the carotid arteries and jugular veins. Phase difference images also can be used to detect retrograde flow in vessels such as in vertebral steal syndrome.

So, with phase difference images, vascular anatomy can be assessed, and the speed and direction of the blood flow can be qualitatively and quantitatively evaluated. In addition, if the images demonstrate the vessel cross section, quantitative information regarding the volume flow rate of the blood can be derived. To determine the volume flow rate, computer software is used to calculate the product of the vessel area and the average velocity over the vessel cross section to yield the volume flow rate (velocity × area = volume flow rate, mm^3/sec). Volume flow rate can be used to determine the effect of pathology by comparing flow on the contralateral side to that on the ipsilateral side, or by comparing flow before and after a physical, or drug-induced, challenge.

In the *complex difference* images, the signal strength is dependent on the velocity of the spins (as it is in phase difference images), but the dependence is not linear as it is in phase difference processing, nor is the direction of blood flow represented. Therefore, complex difference images are not used to determine quantitative information, but are used for demonstrating the anatomy of the vessels, and qualitatively assessing the velocity of blood.

Conventional *magnitude* images also can be constructed from the acquired data because phase contrast techniques do not destroy the magnitude information - they simply alter the phase of the magnetization.

Phase contrast methods are implemented using two-dimensional or three-dimensional acquisition. Two-dimension acquisition can be completed rapidly and is effective for localizing. Two-dimensional acquisition also can be cardiac gated to provide images of the vessels throughout the cardiac cycle. If the cardiac-gated images are acquired perpendicular to the direction of flow, and phase difference processing is performed, flow information throughout the cardiac cycle can be calculated.

Three-dimensional acquisition is considerably more time consuming than two-dimensional acquisition and so it currently is used less frequently. Due to the long scan time associated with three-dimensional acquisition, it currently is not cardiac gated. Benefits of three-dimensional acquisition include an inherently high signal-to-noise ratio, small voxels, and a shorter echo time (TE) than thin-slice two-dimensional acquisition. Also, three-dimensional image sets can be reprojected or reformatted to permit observation of the vessels from any orientation. Images reformatted perpendicular to a vessel can be used to determine volume flow rate through that vessel.

Phase contrast methods are sensitive to a range of velocities. To specify this range of velocities, the user chooses a velocity-encoding (Venc) value. Blood velocities higher than the Venc value will be misrepresented in the image, so the user must choose this value carefully. Some *a priori* information regarding the anticipated pathology may be useful in determining the velocity-encoding value to use. Alternatively, different velocity-encoding values can be used in different scans to highlight different vessels. For example, this is an effective means of producing separate images of the feeding arteries, the draining veins, and the nidus of an arteriovenous malformation, each of which contain blood flowing in different velocity ranges. Acquiring several images using a variety of velocity-encoding values also is useful for demonstrating the fast flow in the in-flow jet of a giant aneurysm in a separate image from the slow stagnant flow in the center of the aneurysm.

In order to encode flow in all directions, a flow-encoding gradient must be applied on each of the three gradient axes in separate TR intervals. In addition, a fourth non-flow-encoded acquisition must be acquired. This non-flow-encoded acquisition is subtracted from each of the three flow-encoded acquisitions to eliminate phase accumulation from sources other than velocity. The subtraction results in high contrast between vessels and stationary tissues, permitting large fields-of-view to be imaged without detrimental effects from saturation, as long as a relatively small tip angle (20°-30°) is used.

The scan time for encoding flow in all directions using two-dimensional acquisitions is $4 \times TR \times NSA \times \#PE$, where NSA is the number of signal averages, and #PE is the number of phase-encoding values acquired. If flow is encoded in only a single direction, the factor of four is reduced to a factor of two. With two-dimensional acquisitions, typically a single thick slab is imaged. If multiple slabs were imaged, the above equation would have to be multiplied by the number of slabs. The scan time for encoding flow in all directions using three-dimensional acquisitions is $4 \times TR \times NSA \times \#PE \times \#SE$, where #SE is the number of slice-encoding values acquired and all other abbreviations are as described above.

Time-of-flight techniques derive contrast between flowing blood and stationary tissues by manipulating the magnitude of the magnetization, such that the magnitude of the magnetization from the moving spins is large and that from the stationary spins is small. This leads to a large signal from moving blood spins and a diminished signal from stationary tissue spins.

In MR, the signal from spins decreases with exposure to an increasing number of excitation pulses, until eventually a saturation value is reached. In time-of-flight imaging, the goal is to subject the flowing spins to only a very few excitation pulses, while subjecting stationary spins to a large number of excitation pulses. This provides a large signal from flowing blood spins, and a small signal from stationary tissue spins. This can be achieved by imaging slices, or thin slabs, oriented perpendicular to the main direction of flow. When this is done, the

moving spins enter the slice fully magnetized, experience only a few excitation pulses, and then flow out of the slice. This ensures that the signal from the blood will be relatively large because the blood is continuously refreshed during image acquisition, and it, therefore, never experiences enough excitation pulses to become saturated. The stationary tissues, however, remain in the slice, or slab, throughout image acquisition, and so they give rise to a diminished signal because the magnetization from them is saturated due to the constant exposure to the excitation pulses.

The number of excitation pulse experienced by moving spins as they traverse the imaging slice is dependent on the thickness of the slice, the velocity of the blood, the orientation of the vessel, and the TR of the imaging sequence. In general, thinner slices, faster-flowing blood, vessels oriented perpendicular to the slice, and a longer TR lead to increased vascular signal. A longer TR, however, also leads to increased signal from stationary tissues, so an intermediate TR is selected. Increasing the tip angle leads to diminished signal from stationary tissues, but it can also lead to increased saturation of blood that experiences multiple excitation pulses, so an intermediate tip angle is typically used. These factors and others must be carefully considered when designing a time-of-flight protocol.

Time-of-flight methods can be implemented using two-dimensional or three-dimensional acquisition. For two-dimensional acquisition, data are acquired from multiple slices stacked contiguously along the vessels of interest. The data from the slices can be reprojected or reformatted to demonstrate long segments of the vessels. With two-dimensional acquisition, the slices are thin (1 – 3 mm), increasing the likelihood that the blood experiences only a very few excitation pulses as it flows through the slice. Thus, a moderately large tip angle (60°) can be used to suppress the signal from the stationary tissues without suppressing the signal from blood. Two-dimensional acquisition can be cardiac gated to reduce signal ghosting, or replication of the vascular signal in images, caused by cardiac pulsatility.

For three-dimensional acquisition, a slab, oriented perpendicular to the vessels of interest, is imaged and the slab is encoded into thin slices using an encoding method similar to that used for phase encoding. Because a slab is imaged, a small tip angle (30°) must be used so the signal from blood that remains in the slab does not become too saturated. The small tip angle necessary to preserve signal from blood also leads to an undesirable preservation of signal from stationary tissues. Therefore, when three-dimensional acquisition is employed, other mechanisms must be implemented in order to reduce the signal from stationary tissues, as described below.

One method employed to diminish signal from stationary tissues in three-dimensional time-of-flight is the use of magnetization transfer. With magnetization transfer, an off-resonance pulse is applied at the start of each TR to saturate the magnetization from restricted water molecules that are bound to macromolecules. Signal from the restricted water molecules does not appear in MR images because the T2 of the signal from these molecules is too short. When the magnetization from these restricted water molecules becomes saturated due to application of the off-resonance pulse, nearby free water molecules can transfer their magnetization to the restricted water molecules, leading to a diminished signal from free water in tissues that contain macromolecules. Grey and white brain matter contain macromolecules whereas blood does not. Thus, magnetization transfer can be used to diminish the signal from the brain, while leaving the signal from blood unaffected, providing increased contrast in intracranial three-dimensional time-of-flight angiograms. Because the magnetization transfer pulse is applied in each TR interval, selecting this feature requires that the TR be increased, resulting in a longer scan time.

Applying a magnetization transfer rf pulse during each TR also leads to an increase in the deposited energy.

The contrast in three-dimensional time of flight angiograms can be further improved by choosing an echo time that ensures that magnetization from fat and water are 180° out of phase with one and other at a critical time during signal detection so that the signals from them cancel each other. Fat and water precess at different rates, so at certain times, the magnetization from them is opposed. At a magnetic field strength of 1.5T, fat and water are at an opposed phase at echo times of 2.3 msec and 6.9 msec. Choosing these echo times is an effective means of suppressing signal from tissues that contain both fat and water.

Another mechanism used to achieve higher contrast between flowing blood and stationary tissues in three-dimensional acquisition is the use of a ramped tip angle. A ramped tip angle is used to reduce the saturation of blood signal as the vessels penetrate farther into the slab. The tip angle is ramped such that a small tip angle is applied where the vessels of interest enter the slab, and a large tip angle is applied where the vessels of interest exit the slab. The small tip angle at the entrance of the slab prevents the blood from becoming too saturated as it traverses the slab. The large tip angle at the exit of the slab tips a large component of the almost fully saturated blood into the transverse plane to be sampled just before it leaves the slab, providing a larger signal than would be achieved by using a small tip angle. The large tip angle saturates the blood, but this is inconsequential, since the saturated blood will exit the slab. The ramped tip angle provides a more uniform signal along the vessels as they traverse the slab, provided they follow a fairly direct path through the slab. A drawback of this imaging feature is that vessels that run parallel to the edge of the slab in the region of the large tip angle may become saturated.

Even with these imaging features, contrast between blood and stationary tissues can be small in the three-dimensional time-of-flight acquisition, especially when thick slabs are used to achieve adequate coverage. To achieve greater coverage with reduced saturation effects, multiple thin slabs can be imaged. The multi-slab method combines the thin-slice benefits of two-dimensional acquisition with the benefits of three-dimensional acquisition, including an inherently high signal-to-noise ratio, small voxels, and a short TE. Even the multi-slab method can suffer from saturation of slowly flowing blood at the exit of each slab. This saturation effect causes signal diminution at the distal edge of each slab, and is referred to as the slab boundary artifact, or the venetian blind artifact. This artifact often occurs in the slow-flow region of the carotid bulb, and may mimic a stenosis.

With both two-dimensional and three-dimensional acquisition, a spatial saturation pulse can be applied adjacent to the slice, or slab, at the beginning of each TR to eliminate signal from blood that is going to flow into the imaging slice. This is an effective means of eliminating signal from venous blood that is going to flow into the imaging slice, or slab, and if left unsaturated would interfere with observation of arteries.

Cardiac-gated two-dimensional time-of-flight is well suited for imaging the carotid arteries, because they are relatively straight vessels, and the jugular veins can be well suppressed using a saturation pulse. A drawback of two-dimensional time-of-flight is that, due to signal-to-noise ratio considerations and the slice selection process, the imaged slices are relatively thick (1 – 3 mm). Using thick slices leads to relatively poor spatial resolution in the slice direction. The effective resolution can be improved by overlapping the slices. Using thick slices also yields large voxels that each contain a large number of spins. The large voxels, in conjunction with the long echo times inherent with two-dimensional time-of-flight, cause this method to be quite severely affected by phase cancellation of spins (signal loss) near pathologies that produce

complex flow patterns. This sensitivity to complex flow, which manifests as potentially large signal voids, has led to the use of two-dimensional time-of-flight as a screening tool to draw attention to tight stenoses in the carotid arteries.

When it is desirable to obtain an accurate depiction of pathology in the carotid arteries, to facilitate quantitative grading of stenoses, for example, the multi-slab three-dimensional time-of-flight method is used. The multi-slab method, with its high resolution, high SNR, and its many features to improve contrast also is used to assess the intracranial vessels. If a small region is being imaged, such as the circle of Willis, the single slab three-dimensional time-of-flight method is used.

Contrast-enhanced techniques derive signal differences between blood and stationary tissues by manipulating the magnitude of the magnetization, such that the magnitude of the magnetization from moving spins is larger than that from stationary spins. Signal differences in contrast-enhanced techniques are achieved not only by employing the appropriate sequence parameters (as is the case in time-of-flight techniques), but also by injecting a contrast agent intravenously to selectively shorten the T1 of the blood. By implementing a T1-weighted imaging sequence during the first pass of the contrast agent, images can be produced that show arteries with striking contrast relative to surrounding stationary tissues and veins. Contrast enhanced methods have been used successfully to image vessels throughout the body.

Dramatically shortening the T1 of blood causes the blood to give rise to a very large signal when imaged using a T1-weighted imaging sequence. The large blood signal is minimally affected by intravoxel dephasing, which is typically caused by complex flow and susceptibility variations. Because the contrast-enhanced techniques are relatively insensitive to signal loss, they provide high quality images with fewer artifacts than the non-contrast-enhanced methods. Because effects of saturation are minimal, large fields of view can be imaged to demonstrate large vascular areas in a short acquisition time. The short imaging time permits acquisition in a single breath-hold interval, providing high quality images even in areas affected by respiratory motion.

Synchronizing the acquisition with the arrival of the contrast agent is critical to image quality. If the data are acquired before the arrival of the contrast agent, the vessels will not appear in the image. If the data are acquired too late, the arterial signal will be diminished, and the veins and stationary tissues will be enhanced.

Several methods have been developed to ensure proper timing of the acquisition relative to the passage of the contrast agent. In one method, a 1-2 ml bolus of contrast agent is injected, and then two-dimensional images are rapidly and repeatedly acquired. From these images the arrival time of the contrast agent can be determined and used to calculate when to start the acquisition of the three-dimensional angiogram after injecting the full bolus. Other methods monitor the signal in a volume or an image and begin acquisition of the angiogram when it has been determined that the contrast agent has arrived. Two- and three-dimensional time-resolved angiographic methods also can be used to continuously image during the passage of the contrast agent. In addition to demonstrating the peak arterial frame, time-resolved methods provide some information regarding the hemodynamics.

A current challenge of contrast-enhanced MR angiography is obtaining high enough spatial resolution in the short amount of time available between arterial and venous enhancement. To address this issue, sequences have been developed that modify the acquisition order to acquire the low spatial frequency data early, during arterial enhancement, and the high

spatial frequency data later, during venous enhancement. The low spatial frequencies contain the bulk of the image contrast information, whereas the high spatial frequencies contain the vessel edge information. Acquiring the low spatial frequency information early reduces the amount of venous signal in the images. These methods are named for their data acquisition order, and are referred to as elliptical centric phase encoding order methods.

Contrast agents that remain in the blood pool for several hours, without leaking into the surrounding stationary tissues, have been developed recently and currently are being evaluated. These so called intravascular agents can be used to increase the imaging time in order to get greater coverage and greater spatial resolution. The drawback of increased acquisition time is that it results in venous enhancement, which leads to difficulty in evaluating the arteries. Methods are being developed to separate arterial signal from venous signal. These methods are not yet available clinically. An additional benefit of some of the intravascular agents is that they have a greater relaxivity. In other words, they provide greater vascular signal during the first pass of the contrast agent by causing a more dramatic decrease in the T1 of blood as compared to some of the existing extravascular contrast agents.

All of the MR angiographic methods are benefiting from advances in coil design. There are a number of multi-element coils available that provide greater coverage than is available from single element coils. Multi-element coil arrays also provide higher signal-to-noise ratios than single element coils. Higher field strength scanners (3 T) also provide higher signal-to-noise ratios. The prevalence of these scanners is increasing, and initial MRA acquisitions demonstrate very high quality results. Additionally, several novel acquisition and processing methods have recently been developed that permit a reduction in scan time by factors of between 2 and 4. These methods are gaining widespread acceptance. They employ the sensitivity of the different elements of multi-element receiver coils to aid in spatial localization of signal, thereby reducing the number of phase encoding steps that need to be acquired during imaging. These so called parallel imaging methods are referred to as SENSE or GRAPPA techniques. In exchange for increased acquisition speed, these methods suffer from reduced signal-to-noise ratios, so they may be better suited for imaging at higher field strengths.

Many of the MR angiographic methods are using a relatively recently introduced feature referred to as zero filling. Zero filling is a reconstruction feature that improves the apparent resolution of images, both within the imaging plane, and in the slice direction with three-dimensional methods. Because it is applied during reconstruction, it does not affect the scan time. When this feature is used, zeroes are applied to the edge of data space prior to reconstruction. When zero filling is used in the frequency- or phase-encoding directions, the result is insertion of pixels between the original pixels in the image. The original pixels are unmodified. The inserted pixels contain data that is interpolated between adjacent (original) pixels. The interpolation is non-linear, meaning that the interpolated values can be greater or less than the average value of the adjacent (original) pixel values. The result is that zero filling makes vessels appear smoother by reducing the stair-step effect and can permit better distinction of small vessels that are very close together. When zero filling is applied in the slice encoding direction for three-dimensional applications, the original slices remain the same, but interpolated slices are inserted between each pair of adjacent slices. This results in smoother appearing vessels in the reformatted and reprojected images.

When properly implemented, all of the MR angiographic methods can yield diagnostic-quality images. The objective of this presentation is to introduce some of the physical principles that affect image quality, so that they can be understood and utilized to consistently obtain diagnostic images.